REMARKS

Claims 28-32 have been cancelled. Claims 5 and 14 have been amended. Claims 5, 9, 12, 14, and 16 are now before the Examiner. The amendments have been made to clarify the claimed subject matter and to correct typographical errors. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Corrections to the specification

The specification at page 18, line 27 has been corrected to insert the SEQ ID NOS. of the primers. The specification at page 20 has been corrected to change "n°" to "No." A typographical error has been corrected.

Formal drawings

Formal drawings were submitted with the Amendment of June 13, 2003.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 5, 9, 12, 14, and 16 are rejected under 35 U.S.C. § 112, first paragraph because the specification, while being enabling for two human polynucleotides consisting of SEQ ID NO: 1 and 10, a rat polynucleotide of SEQ ID NO: 3 and a mouse polynucleotide of SEQ ID NO: 5 that encode peroxisomal -associated polypeptides corresponding to SEQ ID NOS: 2, 4, and 6, respectively, and polynucleotide probes of SEQ ID NOS: 7-9, and 11-16 for in vitro diagnosis, does not enable the skilled art worker to make and use the invention for the scope as claimed.

The Examiner has stated that the specification is enabling for human polynucleotides consisting of SEQ ID NO:1. Claim 5 has been amended to recite an isolated or purified polynucleotides ***consisting of*** SEQ ID NO:1 or its complementary strand. The subject matter of claim 5 is clearly enabled by the specification, which discloses a human polynucleotide, having SEQ ID NO:1. Applicants kindly request withdrawal of the claim rejection on this basis.

Claim 9 recites a vector comprising the polynucleotide of claim 5. Claim 14 refers to a pharmaceutical composition comprising the nucleotide sequence of claim 5. Claim 16 refers to a cell transformed by the vector according to claim 9.

While the Examiner has conceded that SEQ ID NO: 1 is enabled by the specification, the Examiner maintains that claims drawn to a pharmaceutical composition comprising the polynucleotide sequence of SEQ ID NO: 1 are not enabled because the inventors have not demonstrated a dose-dependent neuroprotection against excitotoxic brain lesions by peroxiredoxin 5. This ground of rejection is traversed by Applicants' first example, discussed below, which shows that the systemic administration of recombinant peroxiredoxin 5 to mice induced a dose-dependent neuroprotection against excitotoxic brain lesions.

The Examiner further states that a pharmaceutical composition is unpredictable because (1) the efficacy of gene therapy has not been demonstrated, (2) it is not always possible to extrapolate from in vitro diagnostic experiments to in vivo treatment (3) high level expression of genes may not persist (4) appropriate expression of polynucleotide transfer to specific cell types has not been demonstrated, (5) adverse reactions may occur, and (6) gene transfer with naked DNA has low efficiency.

In response, means to deliver genetic material for therapeutic purposes were known at the time of the claimed invention, as demonstrated by the patent document (U.S. Patent No. 6,468,798) submitted with the Amendment of June 13, 2003 as Attachment A. The '798 patent describes delivery of genetic material for in vivo gene therapy, particularly delivery to the lung for pulmonary disorders. Thus, means to introduce genetic material into mammals were known. The lengthy listing of cited prior art in the front of the '798 patent also attests to the fact that methods of ex vivo gene transfer were well known. Thus, it was well within the skill level in the art to use the polynucleotide of claim 5 in a pharmaceutical composition for gene delivery.

Furthermore, Applicants' claimed composition does not need to work perfectly in order to meet the requirements of 35 U.S.C. § 112, first paragraph. Thus, the Examiner's concerns that high level expression may not persist or that adverse reactions may occur or that the efficiency may be low are misplaced. Clearly, gene delivery by a variety of means with a measurable level of expression in the target cell was not out of reach at the time of the claimed invention.

Furthermore, PRDX5 in PBS is an example of a pharmaceutical composition, comprising a pharmaceutically acceptable carrier (PBS) and the nucleotide sequence of claim 5, which

encodes a polypeptide (PRDX5). Consequently, claims drawn to a pharmaceutical composition are fully supported and enabled by the present specification.

The following examples, which were also previously submitted in reply to the Office Action of June 18, 2002, are presented. In the first example, the Examiner's concern that a dose-dependent neuroprotection against excitotoxic brain lesions by peroxiredoxin has not been demonstrated is directly addressed.

Peroxiredoxin PRDX 5 (PRDX5) belongs to a family of peroxidases widely distributed in eukaryotes and prokaryotes, the peroxiredoxins. The sequence encoding PRDX5 (Accession no NM_012094) 100% corresponds to SEQ ID NO:1 sequence.

In a first example, the inventors have demonstrated that the systemic administration of recombinant peroxiredoxin 5 to mice induced a dose-dependent neuroprotection against excitotoxic brain lesions. In this example, human PRDX5 cDNA (sequence identical to SEQ ID NO:1) was PCR amplified. The PCR product was digested and further ligated into the pQE-30 expression vector. The resulting vector was used to transform *Escherichia coli* strain M15 (pRep4). Bacteria were grown, pelleted cells were lysed by sonication and clarified by centrifugation. The supernatant containing the recombinant PRDX5 was loaded on a column and eluted. The eluted protein was then dialysed against PBS. Excitotoxic brain lesions were induced by intracerebral injection of ibotenate into developing mouse brains. Recombinant PRDX5 (0.1-20 mg/kg) was administered by intraperitoneal injection. Systemically administered PRDX5 induced a dose-dependent neuroprotection of the excitotoxic brain lesions.

As described above an *E. coli* strain was transformed with a vector comprising the sequence of PRDX5 (identical to SEQ ID NO:1). The above example clearly shows the utility of the presently claimed invention. Applicants assert that the example above demonstrates that one skilled in the art could make and use a vector comprising the polynucleotide of claim 5 as recited in claim 9 and a cell transformed by a vector as recited in claim 16. Consequently, the present specification is fully enabling for these claims.

Furthermore, claim 5 has been amended to recite that the polynucleotide consists of SEQ ID NO: 1. The above example relates to PRDX5 which corresponds 100% to SEQ ID NO: 1. Consequently, the above example is commensurate in scope with the claims as presently amended.

Applicants further assert that the above-described experiment also enables a pharmaceutical composition as recited in claim 14. The PRDX5 in PBS is an example of a pharmaceutical composition, comprising a pharmaceutically acceptable carrier (PBS) and the nucleotide sequence of claim 5, which encodes a polypeptide(PRDX5).

In addition, in reply to the Office Action of June 18, 2002, a paper was submitted entitled "Overexpression of human peroxiredoxin 5 in Chinese Hamster Ovary cells" wherein is demonstrated that overexpression of PRDX5 in host cells (Chinese hamster ovary cells) decreases the damage induced by peroxides. For convenience, this paper is resubmitted here as Attachment B.

In this paper it is described that Chinese hamster ovary cells are stably transfected with a vector comprising the cDNA sequence of PRDX5 (accession NO NM_012094) which is identical to SEQ ID NO:1. This second example also provides enablement for claims 9 and 16 relating to a vector comprising the polynucleotide consisting of SEQ ID NO:1 and a cell transformed by said a vector, respectively.

This paper illustrates that overexpression of PRDX5 by Chinese hamster ovary cells in cytosolic and mitochondrial compartments increases cell survival of cells challenged by peroxides and that overexpression of PRDX5 in the nucleus decreases DNA damages induced by peroxides. Thus, PRDX5, which is encoded by a sequence 100% identical to SEQ ID NO:1 has been demonstrated herein to have important applications in therapies. Consequently, this example provides a written enablement for claim 14, which relates to a pharmaceutical composition comprising a pharmaceutically acceptable carrier and the nucleotide consisting of SEQ ID NO:1 (PRDX5 sequence). Thus, one skilled in the art would know how to use the polynucleotide of claim 5 as a pharmaceutical composition.

Furthermore, claim 5 has been amended to recite that the polynucleotide consists of SEQ ID NO: 1. The above example relates to PRDX5 which corresponds 100% to SEQ ID NO: 1. Consequently, the above example is commensurate in scope with the claims as presently amended.

Furthermore, claim 12, referring to a diagnostic device comprising the polynucleotide of claim 5, is enabled by example 2 provided in the present patent application. Example 2 illustrates the detection of a polypeptide encoded by the nucleotide consisting of SEQ ID NO:1 of the present invention in different human tissues. For detection of this polypeptide, the nucleotide consisting of SEQ ID NO:1, according to certain aspects of the invention or at least certain portions thereof, is used in a hybridization protocol for diagnosing the presence of the polypeptide encoded by the nucleotide consisting of SEQ ID NO:1. In view hereof, it is believed that a diagnostic device comprising the nucleotide consisting of SEQ ID NO:1 is sufficiently enabled in the present application.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Claims 5, 9, 12, 14, 16, and 32 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) has possession of the claimed invention at the time that the application was filed.

This ground of rejection is believed to be overcome by Applicants' cancellation of claim 32, amendment of claims 5 and 14 and arguments presented above. Withdrawal of the above ground of rejection is respectfully requested.

Claims 5, 9, 12, 14, 16, and 32 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) has possession of the claimed invention at the time that the application was filed. This is a new matter rejection.

This ground of rejection is believed to be moot in view of Applicants' amendment to claim 5. Withdrawal of this ground of rejection is respectfully requested.

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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